



Amoxicillin modulates the intestinal microbiota and impairs the development of oral tolerance to whey – a study in Brown Norway rats

Graversen, Katrine; Bahl, Martin Iain; Larsen, Jeppe Madura; Eriksen, Lise Lotte; Kristensen, Louise; Qvist Stauersbøl, Line; Hornslet, Sofie Emilie; Licht, Tine Rask; Frahm Christoffersen, Heidi; Neergaard Jacobsen, Lotte

Total number of authors:
11

Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):
Graversen, K., Bahl, M. I., Larsen, J. M., Eriksen, L. L., Kristensen, L., Qvist Stauersbøl, L., Hornslet, S. E., Licht, T. R., Frahm Christoffersen, H., Neergaard Jacobsen, L., & Bøgh, K. L. (2018). *Amoxicillin modulates the intestinal microbiota and impairs the development of oral tolerance to whey – a study in Brown Norway rats*. Abstract from 5th Food Allergy and Anaphylaxis Meeting, Copenhagen , Denmark.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Amoxicillin modulates the intestinal microbiota and impairs the development of oral tolerance to whey – a study in Brown Norway rats

Katrine Bækby Graversen¹, Martin Iain Bahl¹, Jeppe Madura Larsen¹, Lise Lotte Eriksen¹, Louise Kristensen¹, Line Qvist Stauersbøl¹, Sofie Emilie Hornslet¹, Tine Rask Licht¹, Heidi Frahm Christoffersen², Lotte Neergaard Jacobsen³, Katrine Lindholm Bøgh¹

1 National Food Institute, Technical University of Denmark, Kgs. Lyngby, Denmark

2 Arla Foods Ingredients, Videbæk, Denmark

3 Arla Foods Ingredients, Viby J, Denmark

Background: Antibiotic use during infancy has been highlighted as a risk factor for development of allergy later in life. However, few studies have investigated the effects of antibiotics on tolerance development. In the present study we investigated how administration of the commonly used antibiotic amoxicillin (AMX) impacts on tolerance development to whey.

Method: Brown Norway (BN) rats (n=12/group) were gavaged daily with either AMX or water for 4 weeks. After one week of AMX treatment, rats were given a whey based hydrolysed infant formula (IF) *ad libitum* in drinking water for 3 weeks. Rats were subsequently post-immunised i.p. with whey once a week for 4 weeks to assess tolerance induction. Elicitation was measured by *in vivo* tests. Whey-specific IgG1 and IgE were quantified in serum, and total and specific IgA in faeces by means of ELISAs. In parallel the microbial composition of ileum, cecum and faeces was analysed by high throughput 16S rRNA gene sequencing after one week of AMX treatment. T and B cells from intestinal tissues and blood were analysed by flow cytometry.

Results: After one week of AMX treatment, corresponding to the time of tolerance induction initiation, the faecal and cecal microbiota showed significantly reduced alpha diversity and observed shifts in compositions were similar to those previously reported in atopic infants. Changes included a reduction in relative abundance of the genera *Lactobacillus* and *Bifidobacterium* and a general reduction in firmicutes compared to untreated controls. Conversely, the genera *Bacteroides*, *Escherichia* and *Klebsiella* expanded. Analysis of ileum content revealed a distinct bacterial community composition compared to cecum/faeces. While the effects of AMX generally were similar in ileum compared to cecum/faeces, some genera, including *Bifidobacterium*, was affected by AMX in the opposite direction.

The serum levels of whey-specific IgG1 and IgE after post-immunisations were higher in rats treated by AMX compared to those not treated by antibiotic. This effect persisted over time. AMX increased total faecal IgA, and increased the frequency of regulatory CD25+FoxP3+ T helper cells in lamina propria.

Conclusion: AMX impaired *de novo* tolerance induction by whey based hydrolysed IF, and resulted in higher levels of specific IgG1 and IgE after post-immunisations. AMX affected both the humoral and cellular immune system in the gut. These effects are likely due to modulation of the intestinal microbiota.